What is claimed:

1. A method of producing a high mannose glucocerebrosidase (hmGCB), comprising:

providing a cell which is capable of expressing glucocerebrosidase (GCB); and

allowing production of GCB having a precursor oligosaccharide under conditions which prevent the removal of at least one mannose residue distal to the pentasaccharide core of the precursor oligosaccharide of GCB, to thereby produce an hmGCB preparation.

2. The method of claim 1, wherein removal of one or more α 1,2 mannose residue(s) distal to the pentasaccharide core is prevented.

3. The method of claim 1, wherein removal of one α 1,3 mannose residue distal to the pentasaccharide core is prevented.

4. The method of claim 1, wherein removal of one α 1,6 mannose residue distal to the pentasaccharide core is prevented.

5. The method of claim 1, wherein said method comprises contacting the cell with a substance which prevents the removal of at least one mannose residue distal to the pentasaccharide core of the precursor oligosaccharide of GCB.

6. The method of claim 5, wherein the substance is a mannosidase inhibitor.

7. The method of claim 6, wherein the mannosidase inhibitor is a class 1 processing mannosidase inhibitor.

8. The method of claim 6, wherein the mannosidase inhibitor is a class 2 processing mannosidase inhibitor.

9. The method of claim 7, wherein the class 1 processing mannosidase inhibitor is selected from the group consisting of: kifunensine, deoxymannojirimycin, and a combination thereof.

10. The method of claim 7, wherein the class 1 processing mannosidase inhibitor is kifunensine.

11. The method of claim 8, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin, 6-deoxy DIM, 6-deoxy-6-fluoro-DIM and combinations thereof.

12. The method of claim 8, wherein the class 2 processing mannosidase inhibitor is swainsonine.

13. The method of claim 6, wherein the mannosidase inhibitor is present at a concentration between about 0.05 to 20.0 μg/ml.

14. The method of claim 13, wherein the mannosidase inhibitor is present at a concentration between about 0.1 to 2.0 μg/ml

15. The method of claim 7, further comprising contacting the cell with a class 2 processing mannosidase inhibitor.

16. The method of claim 15, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin and a combination thereof.

17. The method of claim 15, wherein the class 2 processing mannosidase inhibitor is swainsonine.

18. The method of claim 1, wherein the cell is a knockout for at least one mannosidase.

19. The method of claim 18, wherein the cell is a knockout for a class 1 processing mannosidase.

20. The method of claim 18, wherein the cell is a knockout for a class 2 processing mannosidase.

21. The method of claim 18, wherein the cell is a knockout for a class 1 processing mannosidase and a class 2 processing mannosidase.

22. The method of claim 1, wherein the cell comprises an antisense mannosidase molecule.

23. The method of claim 22, wherein the antisense molecule is selected from the group consisting of: a class 1 processing mannosidase antisense molecule, a class 2 processing mannosidase antisense molecule, both a class 1 processing mannosidase antisense molecule and a class 2 processing mannosidase antisense molecule.

24. The method of claim 1, wherein the hmGCB comprises a carbohydrate chain having at least four mannose residues.

25. The method of claim 24, wherein the hmGCB has at least one carbohydrate chain having five mannose residues.

26. The method of claim 24, wherein the hmGCB has at least one carbohydrate chain having eight mannose residues.

27. The method of claim 24, wherein the hmGCB has at least one carbohydrate chain having nine mannose residues.

28. The method of claim 1, wherein the hmGCB produced has a ratio of mannose residues to GlcNAc residues which is greater than 3 mannose residues to 2 GlcNAc residues.

29. The method of claim 1, wherein the removal of one or more mannose residues distal to the pentasaccharide core is prevented on at least two of the carbohydrate chains of hmGCB.

30. The method of claim 1, wherein at least 60% of the hmGCB of the preparation have one or more carbohydrate chains in which the removal of one or more mannose residues distal to the pentasaccharide core has been prevented.

31. The method of claim 1, wherein the cell comprises an exogenous nucleic acid sequence comprising a GCB coding region.

32. The method of claim 31, wherein the cell further comprises an exogenous regulatory sequence which functions to regulate expression of the GCB coding region.

33. The method of claim 1, wherein the cell comprises an exogenous regulatory sequence which functions to regulate expression of an endogenous GCB coding sequence.

34. The method of claim 1, wherein the cell is a primary cell.

35. The method of claim 1, wherein the cell is a secondary cell.

36. The method of claim 1, wherein the cell is a mammalian cell

37. The method of claim 36, wherein the cell is a human cell.

38. The method of claim 37, wherein the cell is a fibroblast or a myoblast.

39. The method of claim 37, wherein the cell is an immortalized cell.

40. The method of claim 39, wherein the cell is an HT-1080 cell.

41. The method of claim 1, wherein a population of cells which are capable of expressing GCB is provided, and at least 10% of the cells produce GCB with four carbohydrate chains having the specified number of mannose residues.

42. The method of claim 5, wherein the cell is cultured in culture medium comprising at least one mannosidase inhibitor.

43. The method of claim 42, wherein the mannosidase inhibitor is a class 1 processing mannosidase inhibitor.

44. The method of claim 43, wherein the class 1 processing mannosidase inhibitor is selected from the group consisting of: kifunensine, deoxymannojirimycin, and a combination thereof.

45. The method of claim 42, wherein the mannosidase inhibitor is a class 2 processing mannosidase inhibitor.

46. The method of claim 45, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin, 6-deoxy-DIM, 6-deoxy-6-fluoro-DIM, and combinations thereof.

47. The method of claim 43, wherein the medium further comprises a class 2 processing mannosidase inhibitor.

48. The method of claim 42, wherein the hmGCB is obtained from the media in which the cell is cultured.

49. A method of producing high mannose glucocerebrosidase (hmGCB), comprising:

providing a cell which is capable of expressing glucocerebrosidase (GCB); and

allowing production of GCB having a precursor oligosaccharide under conditions which inhibit a class 1 processing mannosidase activity and a class 2 processing mannosidase activity such that the removal of at least one mannose residue distal to the pentasaccharide core of the precursor oligosaccharide of GCB is prevented, to thereby produce an hmGCB preparation.

50. The method of claim 49, wherein the cell is contacted with a substance which inhibits a class 1 processing mannosidase and a substance which inhibits a class 2 processing mannosidase.

51. The method of claim 49, wherein removal of one or more α 1,2 mannose residue(s) distal to the pentasaccharide core is prevented.

52. The method of claim 49, wherein removal of one α 1,3 mannose residue distal to the pentasaccharide core is prevented.

53. The method of claim 49, wherein removal of one α 1,6 mannose residue distal to the pentasaccharide core is prevented.

54. The method of claim 49, wherein the substance is a class 1 processing mannosidase inhibitor.

55. The method of claim 49, wherein the substance is a class 2 processing mannosidase inhibitor.

56. The method of claim 54, wherein the class 1 processing mannosidase inhibitor is selected from the group consisting of: kifunensine, deoxymannojirimycin, and combinations thereof.

57. The method of claim 55, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin, 6-deoxy-DIM, 6-deoxy-6-fluoro-DIM, and a combination thereof.

58. The method of claims 56 or 57, wherein the mannosidase inhibitor is present at a concentration between about 0.05 to 20.0 μg/ml.

59. The method of claim 49, wherein the cell is a knockout for a class 1 processing mannosidase.

60. The method of claim 49, wherein the cell is a knockout for a class 2 processing mannosidase.

61. The method of claim 49, wherein the cell is a knockout for both a class 1 processing mannosidase and a class 2 processing mannosidase.

62. The method of claim 49, wherein the cell comprises a class 1 processing mannosidase antisense molecule.

63. The method of claim 49, wherein the cell comprises a class 2 processing mannosidase antisense molecule.

64. The method of claim 63, wherein the cell comprises a class 1 processing mannosidase antisense molecule and a class 2 processing mannosidase antisense molecule.

65. The method of claim 49, wherein the cell comprises an exogenous nucleic acid sequence comprising a GCB coding region.

66. The method of claim 65, wherein the cell further comprises an exogenous regulatory sequence which functions to regulate expression of the GCB coding region.

67. The method of claim 49, wherein the cell comprises an exogenous regulatory sequence which functions to regulate expression of an endogenous GCB coding sequence.

68. The method of claim 50, wherein the cell is cultured in a culture media comprising at least one class 1 processing mannosidase inhibitor and at least one class 2 processing mannosidase inhibitor.

69. The method of claim 68, further comprising obtaining the hmGCB from the media in which the cell is cultured.

70. A method of producing high mannose glucocerebrosidase (hmGCB), comprising:

providing a cell into which a nucleic acid sequence comprising an exogenous regulatory sequence has been introduced such that the regulatory sequence regulates the expression of an endogenous GCB coding region; and

allowing production of GCB having a precursor oligosaccharide under conditions which prevent the removal of at least one mannose residue distal to the pentasaccharide core of the precursor oligosaccharide of GCB, to thereby produce an hmGCB preparation.

71. A high mannose glucocerebrosidase (hmGCB) preparation comprising at least one carbohydrate chain having at least four mannose residues of a precursor oligosaccharide chain.

72. The hmGCB preparation of claim 71, wherein the hmGCB has at least one carbohydrate chain having five mannose residues.

73. The hmGCB preparation of claim 71, wherein the hmGCB has at least one carbohydrate chain having eight mannose residues.

74. The hmGCB preparation of claim 71, wherein the hmGCB has at least one carbohydrate chain having nine mannose residues.

75. The hmGCB preparation of claim 71, wherein the hmGCB produced has at least one carbohydrate chain having a ratio of mannose residues to GlcNAc residues which is greater than 3 mannose residues to 2 GlcNAc residues.

76. The hmGCB preparation of claim 71, wherein at least two of the carbohydrate chains of hmGCB have at least four mannose residues of the precursor oligosaccharide chain.

77. The hmGCB preparation of claim 71, wherein at least 85% of the hmGCB of the preparation have four carbohydrate chains in which the removal of one or more mannose residues distal to the pentasaccharide core has been prevented.

78. A pharmaceutical composition, comprising:

the hmGCB preparation of claim 71, in an amount suitable for treating Gaucher disease.

79. The composition of claim 78, further comprising a pharmaceutically acceptable carrier or diluent.

80. A method of treating a subject having Gaucher disease, comprising:

administering to the subject the composition of claim 78, to thereby treat Gaucher disease.

81. A method of purifying hmGCB from a sample, comprising:

providing a harvested hmGCB product; and

subjecting the hmGCB product to hydrophobic charge induction chromatography (HCIC) or hydrophobic interaction chromatography (HIC),

thereby obtaining purified hmGCB.

82. The method of claim 81, wherein MEP Hypercel® is used for HCIC.

83. The method of claim 81, wherein MacroPrep Methyl® is used for HIC.

84. The method of claim 81, further comprising subjecting the hmGCB product to ion exchange chromatography.

85. The method of claim 84, wherein the hmGCB product is subjected to HCIC or HIC prior to ion exchange chromatography.

86. The method of claim 84, wherein the hmGCB product is subjected to ion exchange chromatography prior to HCIC or HIC.

87. The method of claim 84, wherein the hmGCB product is subjected to more than one ion exchange chromatography step.

88. The method of claim 84, wherein the ion exchange chromatography is selected from the group consisting of anion exchange chromatography and cation exchange chromatography.

89. The method of claim 88, wherein anion exchange chromatography is performed using one or more of: Q Sepharose Fast Flow®, MacroPrep High Q Support®, DEAE Sepharose Fast Flow®, and Macro-Prep DEAE®.

90. The method of claim 88, wherein cation exchange chromatography is performed using one or more of: SP Sepharose Fast Flow®, Source 30S®, CM Sepharose Fast Flow®, Macro-Prep CM Support®, and Macro-Prep High S Support®.

91. The method of claim 84, further comprising subjecting the hmGCB product to size exclusion chromatography.

92. The method of claim 91, wherein the size exclusion chromatography is performed using one or more of: Superdex 200®, Sephacryl S-200 HR® and Bio-Gel A 1.5m®.

93. A method of purifying hmGCB, comprising:

providing a harvested hmGCB product;

subjecting the hmGCB product to hydrophobic charge induction chromatography (HCIC) or hydrophobic interaction chromatography (HIC); and

subjecting the hmGCB product to one or more of anion exchange chromatography, cation exchange chromatography, and size exclusion chromatography,

thereby obtaining purified hmGCB.

94. The method of claim 93, wherein MEP Hypercel® is used for HCIC.

95. The method of claim 93, wherein MacroPrep Methyl® is used for HIC.

96. The method of claim 93, wherein anion exchange chromatography is performed using one or more of: Q Sepharose Fast Flow®, MacroPrep High Q Support®, DEAE Sepharose Fast Flow®, and Macro-Prep DEAE®.

97. The method of claim 93, wherein cation exchange chromatography is performed using one or more of: SP Sepharose Fast Flow®, Source 30S®, CM Sepharose Fast Flow®, Macro-Prep CM Support®, and Macro-Prep High S Support®.

98. The method of claim 93, wherein the size exclusion chromatography is performed using one or more of: Superdex 200®, Sephacryl S-200 HR® and Bio-Gel A 1.5m®.

99. A method of purifying hmGCB, comprising:

providing a harvested hmGCB product;

subjecting the hmGCB product to hydrophobic charge induction chromatography (HCIC) or hydrophobic interaction chromatography (HIC);

subjecting the HCIC or HIC purified hmGCB product to anion exchange chromatography;

subjecting the anion exchange purified hmGCB to cation exchange chromatography; and,

subjecting the cation exchange purified hmGCB to size exclusion chromatography, thereby obtaining purified hmGCB.

100. The method of claim 99, wherein MEP Hypercel® is used for HCIC.

101. The method of claim 99, wherein MacroPrep Methyl® is used for HIC.

102. The method of claim 99, wherein anion exchange chromatography is performed using one or more of: Q Sepharose Fast Flow®, MacroPrep High Q Support®, DEAE Sepharose Fast Flow®, and Macro-Prep DEAE®.

103. The method of claim 99, wherein cation exchange chromatography is performed using one or more of: SP Sepharose Fast Flow®, Source 30S®, CM Sepharose Fast Flow®, Macro-Prep CM Support®, and Macro-Prep High S Support®.

104. The method of claim 99, wherein the size exclusion chromatography is performed using one or more of: Superdex 200®, Sephacryl S-200 HR® and Bio-Gel A 1.5m®.

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